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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/049,762	06/20/2002	Alexander James Bridges	A0000100-01-SMH	7601

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EXAMINER	
JIANG, SHAOJIA A	

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 02/17/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/049,762	BRIDGES ET AL.	
	Examiner	Art Unit	
	Shaojia A Jiang	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 December 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-125* is/are pending in the application.

4a) Of the above claim(s) *1-58,95-123 and 125* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *59-94 and 124* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This application is a 371 (a national stage entry) of PCT/US00/18348 International Filing Date: 07/05/2000.

Election/Restrictions

Applicant's election without traverse of the invention of Group IV, claims 59-94 and 124 drawn to a method of treating pain employing a compound of formula IB, and the species of compound 2-(2-chloro-4-ethynyl-phenylamino)-N-cyclopropylmethoxy-3,4-difuoro-benzamide, submitted December 8, 2003 is acknowledged.

On consideration by the examiner, the specie election requirement is modified to include all compounds covered by Formula (I)B in claim 59 as a single specie, elected by Applicant December 8, 2003.

Claims 1-58, 95-123 and 125 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Claims 59-94 and 124 will be examined on the merits herein.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 59-60, 62, 63, 68-94 and 124 are rejected under 35 U.S.C. 112, first paragraph, for scope of enablement because the specification, while being enabling the instant compounds for treating particular chronic pain caused by the particular diseases/disorders, does not reasonably provide enablement for treating any chronic pain caused by any diseases/disorders.

The instant specification fails to provide information that would allow the skilled artisan to fully practice the instant invention without ***undue experimentation***. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

(1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

The nature of the invention: The instant invention pertains to a method of treating chronic pain.

The relative skill of those in the art: The relative skill of those in the art is high.

The breadth of the claims: The instant claims are deemed very broad since these claims reads on treating any disease states or conditions associated with pain and the symptoms associated pain.

Regarding the *Wands* factor (4) the predictability or unpredictability of the art:

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. *In re Fisher*, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. In the instant case, the instant claimed invention is highly unpredictable since one skilled in the art would recognize that the recitation encompasses any disease states or conditions associated with pain and the symptoms associated pain, a great numbers of diseases or disorders such as inflammatory pain, neuropathic pain, and pain caused by migraine, tension headache, cluster headade, and bowel disorder, diopathic pain, and pain associated with chronic alcoholism, vitamin deficiency, uremia, or hypothyroidism, which are known to be *involved various, many possible, and different, separate and independent etiologies*. Thus, the skilled artisan would view that the treatment of all conditions associated with pain and the symptoms associated pain by administering the particular compound herein is highly unpredictable.

Moreover, one of skill in the art would recognize that it is highly unpredictable in regard to therapeutic effects, side effects and toxicity generated by administering the instant compound for treating any conditions encompassed by the claims herein.

In regard to these *Wands* factors, (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary:

It is noted that merely several particular compounds within the claims, i.e., PD219622, PD297447, PD 184352, PD 254552 were administered intrathecally to a

neuropathic pain model in the rat shown at Example 3 of the specification. Thus, the evidence in the examples is not commensurate in scope with the claimed invention and does not demonstrate criticality of a wide spectrum of disease states associated pain in the claimed method and a claimed range of the compounds. See MPEP § 716.02(d).

Thus, the specification fails to provide clear and convincing evidence in sufficient support of the broad treatment of any conditions recited in the instant claims. As a result, necessitating one of skill to perform an exhaustive search for the embodiments of treating any conditions recited in the instant claims suitable to practice the claimed invention.

Genentech, 108 F.3d at 1366, states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the *Wands* factors, and *In re Fisher* (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in *undue experimentation* to test all compounds encompassed in the instant claims and their combinations to be administered to a host employed in the claimed methods of the particular treatments herein, with no assurance of success.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 59-94 and 124 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recitation "a subject" renders these claims indefinite. The recitation "a subject" is not clearly defined in the claims or specification. One of ordinary skill in the art could interpret that the term " subject " would be a single cell, any biological system, an animal or a human. Thus, one of ordinary skill in the art could not interpret the metes and bounds of the patent protection desired as to what "a subject" encompassed thereby.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 59, 62, 65-66, 69, and 71 are rejected under 35 U.S.C. 102(b) as being anticipated by Connor et al. (EP 0 316 630 A, WARNER-LAMBERT Co, PTO-1449 submitted May 16, 2003)

Connor et al. discloses that the active compounds of formula I which read on the instant compounds (see particularly page 5-6, e.g. Example 13 and 18), being cycloxygenase inhibitors, are useful in pharmaceutical compositions and methods for

treating inflammation, arthritis, and pain (see abstract, page 4 lines 35—37, page 7-8, and claims 1-17).

Thus, the disclosure of Connor et al. anticipates claims 59, 62, 65-66, 69, and 71.

Claims 59, 62, 65, and 70 are rejected under 35 U.S.C. 102(b) as being anticipated by FUJIMURA H et al.: "HYDCOXAYIC ACID DEZIVATIVES" CHEMICAL ABSTRACTS + INDEXES, AMERICAN CHEMICAL SOCIETY. COLUM8US,US, vol. 70, no. 3 20 January 1966 (1969-01-20), or JP 42 024578 A or JP 42019583 B4 (TAKEDA CHEMICAL INDUSTRIAL LTD, 1967, PTO-1449 submitted May 16, 2003).

FUJIMURA H et al. discloses that the active compounds of formula I which read on the instant compounds (see particularly abstract), are useful as analgesics. Thus, these compounds are useful in pharmaceutical compositions and methods for treating pain (see abstract).

Thus, the disclosure of FUJIMURA H et al. anticipates claims *59, 62, 65, and 70.*

Claims 59, 62, 65, and 69 are rejected under 35 U.S.C. 102(b) as being anticipated by Morkhort (PTO-1449 submitted May 16, 2003)

Morkhort discloses that the active compounds therein which read on the instant compounds (see particularly abstract), are useful as analgesics. Thus, these compounds are useful in pharmaceutical compositions and methods for treating pain (see abstract).

Thus, the disclosure of Morkhort anticipates claims *59, 62, 65, and 69.*

Claims 59, 62, 65, 69 and 77 are rejected under 35 U.S.C. 102(b) as being anticipated by Hirano Hiroshi et al. (JP 42019583 B4 .TAKEDA CHEMICAL INDUSTRIAL LTD, 1967, PTO-1449 submitted May 16, 2003).

Hirano Hiroshi et al. discloses that the active compounds therein which read on the instant compounds (see particularly abstract), are useful as analgesics. Thus, these compounds are useful in pharmaceutical compositions and methods for treating pain (see abstract).

Thus, the disclosure of Hirano Hiroshi et al. anticipates claims *59, 62, 65, 69 and 77.*

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 59-94 and 124 are rejected under 35 U.S.C. 103(a) as being unpatentable over Barrett et al. (WO 99/01421, PTO-1449 submitted May 16, 2003) in view of Walker et al. BRITISH JOURNAL OF CLINICAL PHARMACOLOGY, (1993 Nov) 36 (5) 417-25, PTO-892) and Ma et al. (BRAIN RESEARCH, (1991 Dec 6) 566 (1-2) 95-102, PTO-892).

Barrett et al. discloses that the active compounds of formula I which read on the instant compounds, have covered the instant compounds, or are structurally substantially similar to the instant compounds (see particularly Formula II, III and IIIa at page 5-6, and e.g. Example 212), being MEK inhibitors, are useful in pharmaceutical compositions and methods for treating inflammation (see abstract, page 1-3, and claims 1-34).

Barrett et al. do not expressly disclose the employment of the particular MEK inhibitors therein, in methods of treating chronic pain.

Ma et al. teaches that pain (e.g., neuropathic pain) is known to be associated with MEK. See "abstract" in particular.

Walker et al. teaches that pain is well-known to be associated with inflammation. See "abstract" in particular.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to employ the particular MEK inhibitors of Barrett et al. in methods of treating chronic pain.

One having ordinary skill in the art at the time the invention was made would have been motivated to employ the particular MEK inhibitors of Barrett et al. in methods of treating chronic pain, because particular MEK inhibitors of Barrett et al. is known to be useful in methods of inflammation according to Barrett et al. It is also known that pain (e.g., neuropathic pain) is known to be associated with MEK according to Ma et al. Moreover, pain is well-known to be associated with inflammation.

Further, some of the instant compounds read on the compounds of Barrett et al. while other the instant compounds have been covered by the formula of Barrett et al., or are structurally substantially similar to. As noted in MPEP 2144, "If such a species or subgenus is structurally similar to that claimed, its disclosure may motivate one of ordinary skill in the art to choose the claimed species or subgenus from the genus, based on the reasonable expectation that structurally similar species usually have similar properties. See, e.g., Dillon, 919 F.2d at 693, 696, 16 USPQ2d at 1901, 1904. See also Deuel, 51 F.3d at 1558, 34 USPQ2d at 1214. The utility of such properties will normally provide some motivation to make the claimed species or subgenus. Id. Dillon, 919 F.2d at 697, 16 USPQ2d at 1904-05 (and cases cited therein). If the claimed invention and the structurally similar prior art species share any useful property, that will generally be sufficient to motivate an artisan of ordinary skill to make the claimed species, In fact, similar properties may normally be presumed when compounds are very close in structure. Dillon, 919 F.2d at 693, 696, 16 USPQ2d at 1901, 1904. See also In re Grabiak, 769 F.2d 729, 731, 226 USPQ 870, 871 (Fed. Cir. 1985) ("When chemical compounds have very close' structural similarities and similar utilities, without more a prima facie case may be made."). Thus, evidence of similar properties or evidence of any useful properties disclosed in the prior art that would be expected to be shared by the claimed invention weighs in favor of a conclusion that the claimed invention would have been obvious. Dillon, 919 F.2d at 697-98, 16 USPQ2d at 1905; In re Wilder, 563 F.2d 457, 461, 195 USPQ 426, 430 (CCPA 1977); In re Linter, 458 F.2d 1013, 1016, 173 USPQ 560, 562 (CCPA 1972).

Therefore, one of ordinary skill in the art would have reasonably expected that the particular MEK inhibitors herein, would have beneficial therapeutic effects and usefulness in methods of treating pain caused by the particular disorders/diseases, e.g., neuropathic pain and inflammation, in patents suffering therefrom.

Thus the claimed invention as a whole is clearly prima facie obvious over the combined teachings of the prior art.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 59-94 and 124 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-33 of copending Application No. 10/031149.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the copending application is drawn to the same method of treatment, chronic pain, as the instant claimed method, employing the same or structurally substantially similar to the instant compounds.

Thus, the copending Application No. 10/031149 and the instant claims are seen to substantially overlap.

Thus, the instant claims are seen to be obvious over the all claims of copending Application No. 10/031149.

Claims 59-94 and 124 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over all claims of copending Application No. 10/031037.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the copending application is drawn to the same method of treatment, chronic pain, as the instant claimed method, employing the same or structurally substantially similar to the instant compounds.

Thus, the copending Application No. 10/031037 and the instant claims are seen to substantially overlap.

Thus, the instant claims are seen to be obvious over the all claims of copending Application No. 10/031037.

Above rejections are a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

In view of the rejections to the pending claims set forth above, no claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Jiang, whose telephone number is (571)272-0627. The examiner can normally be reached on Monday-Friday from 9:00 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, Ph.D., can be reached on (571)272-0629. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 305-1235.

S. Anna Jiang, Ph.D.
Patent Examiner, AU 1617
February 7, 2004